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10/821,981	04/12/2004	Seth Orlow	ORLOW1A	3666
1444	7590	09/29/2008		
BROWDY AND NEIMARK, P.L.L.C.			EXAMINER	
624 NINTH STREET, NW			BROWN, COURTNEY A	
SUITE 300				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/821,981	<b>Applicant(s)</b> ORLOW ET AL.
	<b>Examiner</b> COURTNEY BROWN	<b>Art Unit</b> 1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If no period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 05 May 2008.

2a) This action is FINAL.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) 4-15, 24 and 25 is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-3 and 16-23 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement (PTO-1449)  
Paper No(s)/Mail Date 10/27/2004 and 2/28/2005

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_

5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_

**DETAILED ACTION**

Receipt of Amendments/Remarks filed on May 5, 2008 is acknowledged.

After further consideration, the Examiner has discovered that the pending claims are 1-25 instead of claims 1-15. Claims 16-25 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 16-25 are drawn to a method for synthesizing a library of trisubstituted triazines whereas the elected claims are drawn to a method for screening for a test compound.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 4-25 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-3 are being examined for patentability.

***Priority***

Priority to US Provisional Application 60/461,804 filed on April 11, 2003 is acknowledged.

***Information Disclosure Statement***

The Information Disclosure Statements (IDS) submitted on October 27, 2004 and February 28, 2005 have been considered by the examiner.

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/408,108 in view of Ancans et al. and Hopkins et al. Although the conflicting claims

are not identical, they are not patentably distinct from each other because the instantly claimed subject matter embraces or is embraced by the co-pending application.

Copending claim1 teaches the same method of screening compounds that inhibits pigmentation through determining the increase of tyrosinase. The difference between the instant application and copending Application No. 11/408,108 is that the instant application requires the use of a specific trisubstituted triazine compound that interacts with mitochondrial ATPase. However, Ancans et al. teaches that ATPase activates melanogenesis (i.e. pigmentation) through the activation of tyrosinase (see abstract). Hopkins et al. teach that trisubstituted triazine compounds inhibit the activity of kinesin (i.e. ATPase) (see page 5, compound #58616). One would have been motivated to make this combination in order to receive the expected benefit of using trisubstituted triazine compounds to inhibit the activity of ATPase and as result, inhibit pigmentation (i.e. melanogenesis). From this extensive overlap of subject matter, one of ordinary skill in the art would recognize that the same product is produced in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for screening trisubstituted triazines that interact with prohibitin or mitochondrial ATPase, does not reasonably provide enablement for a method for screening other agents that interact with prohibitin or mitochondrial ATPase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without an undue amount of experimentation.

Thus, Applicant is not enabled for a method for screening other agents that interact with prohibitin or mitochondrial ATPase.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the

Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

**1) Scope or breadth of the claims**

The claims are broader in scope than the enabling disclosure. The specification merely discloses, without more, that trisubstituted triazines interact with prohibitin or mitochondrial ATPase. However, Applicant is purporting to use any and all agents that interact with prohibitin or mitochondrial ATPase.

**2) Nature of the invention**

The nature of the invention is directed to a method for screening trisubstituted triazines that interact with prohibitin or mitochondrial ATPase

**3) Relative level of skill possessed by one of ordinary skill in the art**

The relative level of skill possessed by one of ordinary skill in the art of chemical and biological research is relatively high, as a majority of lead investigators directing scientific research and development in this particular technological area possess an Ph.D. in a scientific discipline such as organic synthetic chemistry, polymer chemistry, medicinal chemistry, biochemistry, pharmacology, biology or the like.

**4) State of, or the amount of knowledge in, the prior art**

Hopkins et al. teach that trisubstituted triazine compounds inhibit the activity of kinesin (i.e. ATPase) (see page 5, compound #58616).

**5) Amount of guidance or direction provided by the inventor**

Applicant was required to provide in the specification additional guidance and direction with respect to how use the claimed subject matter in order for the application to be enabled with respect to the full scope of the claimed invention. Although the instant specification discloses that trisubstituted triazines that interact with prohibition or mitochondrial ATPase, it remains silent on the other agents that interact with prohibition or mitochondrial ATPase.

6) Presence or absence of working examples

The specification fails to provide scientific data and working embodiments with respect to other agents other than trisubstituted triazine compounds that interact with prohibition or mitochondrial ATPase,

7) Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

In order to practice the claimed invention, a skilled artisan would have to first determine which other agents contemplated by applicant that interact with prohibitin or mitochondrial ATPase. Since there are very limited working examples as described above, the amount of experimentation will be high and burdensome. Therefore, it would constitute undue experimentation to practice the invention.

Therefore, the breadth of the claims combined with minimal guidance from the specification, the lack of working examples, and lack of predictability, provides for undue experimentation to practice the scope of the instant claims.

Therefore, in view of the Wands factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed

above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the combination in the instant claims whether preventing one or more symptoms of symptoms of diseases or disorders of complications caused by diabetes or associated with diabetes in a human or animal totally, absolutely, or permanently, with no assurance of success.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "other agents" in claim 1 renders the claim indefinite. The term "other agents" is not defined by the claim, the specification does not provide any description, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. As a result, the Examiner does not know the exact identification of the "other agents" that interact with prohibitin or mitochondrial ATPase.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Imokawa (July 1989, Journal of Investigative Dermatology, 93(1):100-7) in view of

Ancans et al. (Federation of European Biochemical Societies, 2000) and Hopkins et al. (Biochemistry, 2000).

***Applicant's Invention***

Applicant claims a method for screening for a test compound being selected from the group consisting of trisubstituted triazines that interact with prohibitin or mitochondrial ATPase and other agents that interact with prohibitin or mitochondrial ATPase to determine if the test compound is one that inhibits or stimulates pigmentation comprising: a.) determining the amount of melanin or tyrosinase in cells or extracts of cells; b. treating the cells with a test compound; and c. determining the amount of melanin or tyrosinase in the treated cells or extracts of cells; d. wherein a change in the amount of melanin or tyrosinase in the cells or the extract of cells in the presence of the test compound as compared to the absence of the test compound indicates that the test compound is one that affects pigmentation.

***Determination of the scope and the content of the prior art  
(MPEP 2141.01)***

Imokawa teaches a method of screening for compounds that inhibit melanogenesis (i.e. a process through which cells produce melanin which is a pigment found in skin), the method comprising: treating mammalian-derived melanocytes or melanoma cells expressing a tyrosinase-encoding gene with a test compound in vitro, and determining the cellular localization of tyrosinase by determining localized

tyrosinase activity in the presence of the test compound, wherein an increase in the amount of tyrosinase found in non-melanosomal vesicles in the presence of the test compound as compared to in the absence of the test compound indicates that the test compound is a candidate for a compound that inhibits melanogenesis (page 106).

***Ascertainment of the difference between the prior art and the claims  
(MPEP 2141.02)***

The difference between the teaching of Imokawa and the invention of the instant application is that the instant application requires the use of a trisubstituted triazine compound that interacts with mitochondrial ATPase. For this reason, the teaching of Ancans et al. and Hopkins et al. are joined. Ancans et al. teaches that ATPase activates melanogenesis (i.e. pigmentation) through the activation of tyrosinase (see abstract). Hopkins et al. teach that trisubstituted triazine compounds inhibit the activity of kinesin (i.e. ATPase) (see page 5, compound #58616).

Another difference between the teaching of Imokawa and the invention of the instant application is that the instant application requires a method indicating that the test compound is a stimulator of pigmentation wherein the amount of melanin in the cells or the extract of cells in the presence of the test compound increases. For this reason, the teaching of Ancans et al. is joined. Ancans et al. teach that ATPase activates melanogenesis (i.e. pigmentation) through the activation of tyrosinase (see abstract).

***Finding of prima facie obviousness***

***Rationale and Motivation (MPEP 2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of the two cited references to arrive at a method for screening for a test compound being selected from the group consisting of trisubstituted triazines that interact with prohibitin or mitochondrial ATPase and other agents that interact with prohibitin or mitochondrial ATPase to determine if the test compound is one that inhibits or stimulates pigmentation. One would have been motivated to make this combination in order to receive the expected benefit of using trisubstituted triazine compounds to inhibit the activity of ATPase and as result, inhibit pigmentation (i.e. melanogenesis). "It would be *prima facie* obvious to combine methods each of which is taught by the prior art to be useful for the same purpose in order to form a resultant method that is to be used for the very same purpose; the idea of combining them flows logically from their having been individually taught in prior art." In re Kerkhoven, 205 USPQ 1069 (C.C.P.A. 1980).

***Examiner's Response to Applicant's Remarks***

Applicant's arguments with respect to claims 1-3 have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

None of the claims are allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR Only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electron Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Courtney Brown, whose telephone number is 571-270-3284. The examiner can normally be reached on Monday-Friday from 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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